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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/876,549	06/07/2001	John SantaLucia JR.	WSU 0192 PUSP	7537

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EXAMINER	
LIN, JERRY	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 12/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/876,549	SANTALUCIA ET AL.	
	Examiner	Art Unit	
	Jerry Lin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-18,20,21,23-37,39-41,43-57 and 59-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-18,20,21,23-37,39-41,43-57 and 59-63* is/are rejected.

7)☒ Claim(s) *18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed August 30, 2005, have been fully considered and they are deemed to be persuasive in-part. In response to the new claims and the amendments, the Examiner has added new grounds of rejection as well as revised previous rejections. For the sake of clarity, the Examiner has also reiterated previous rejections in this office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. This office action constitutes the complete set of rejections and objections presently being applied to the instant application.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See, for example, pages 23 or 26. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

Claim 18 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3-18, 20, 32, 36, 37, 40, 52, 56, 57, and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "a best" in claims 1, 16, 17, 20, 36, 37, 40, 56, 57 and 60 is a relative term which renders the claim indefinite. The term "a best" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is unclear what criteria a practitioner must use in order to determine what is the "best" target/primer or target/probe complex. For purposes of examination, the Examiner will interpret "best" to mean the most thermodynamically stable.

Regarding claims 12, 32, and 52, it is unclear what is meant by top and bottom strand sequences. Nucleic acids typically hybridize in a solution without regard to a top strand or bottom strand. It is unclear what sort of orientation is need to designate one strand as the top and the other strand as the bottom. For purposes of this examination, the Examiner will interpret the claim to mean wherein the hybridization information represents duplexes.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5, 9-18, 20, 21, 23-25, 29-37, 39-41, 43-45, 49-57, and 59-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lange et al. (US 6,403,314) in view of Lane et al. (US 6,027,884).

Regarding claims 1, 21, 39, 41, and 59, Lange et al. discloses a method of predicting the nucleic hybridization in a solution (column 1, lines 15-25; column 3, lines 5-24) which includes providing a database of thermodynamic parameters (column 15, lines 45-58); receiving hybridization information that represents at least one target sequence and a primer and a probe wherein the target sequence is longer than the length of the primer and probe (i.e., a probe hybridizing within a target molecule)

(column 16, lines 1-60; column 3, line 62-column 4, line 59; Figures 5B and 5C; column 5, lines 25-63; column 7,lines 16-29); calculating nucleic acid hybridization thermodynamics including net hybridization thermodynamics based on hybridization information, thermodynamic parameters, hybridization conditions, and correction data (column 11, lines 39-55, column 15, lines 46-58); wherein the nucleic acid hybridization thermodynamics are calculated for a best target/primer or target/ probe complex and for competitive mismatch complexes (column 5, lines 47-63). Furthermore, Lange et al. teach implementing their method using C++ pseudo-code, which would require the use of a computer systems as well as a computer readable storage medium (column 16, line 61-column 17, line 8).

Lange et al., however, do not teach where correction data is received, where the first set of data which represents hybridization conditions is received, or calculating an equilibrium concentration for a species of a molecular complex at a plurality of temperatures, or outputting the equilibrium concentration to an interface.

Also regarding claims 1, 21, 39, 41 and 59, Lane et al. teach a method of determining the thermodynamics of hybridization that includes receiving correction data such as receiving singlet and doublet values to input into a correction factor (column 38, lines 14-61); receiving a set of data that represents hybridization conditions (column 45, lines 21-35; column 48, lines 11-29); calculating an equilibrium concentration for a species of a molecular complex at a plurality of temperatures using statistical weighting and nucleic acid hybridization thermodynamics and outputting the equilibrium concentration (Figure 4, column 9, lines 50-64; column 42, line 43-column 43, line 65).

Regarding claims 3, 11, 23, 31, 43 and 51, Lange et al. teach wherein the correction data includes folding correction data (column 15, lines 4-12).

Regarding claims 4, 24, 44, 61, 62, and 63, Lane et al. teach wherein the correction data includes linear correction data (column 52, line 49-column 53, line 16).

Regarding claims 5, 9, 10, 25, 29, 30, 45, 49, and 50, Lange et al. teach wherein the thermodynamic parameters include DNA, RNA, and DNA/RNA thermodynamic parameters (column 15, lines 18-67).

Regarding claims 12, 32, and 52, Lange et al. teach wherein the hybridization information represents a duplex (column 15, line 17- column 16, line 60).

Regarding claims 13-17, 33-37, and 53-57, Lange et al. teach wherein the hybridization information represents at least a section of the target sequence and a length of at least one primer or probe complimentary to at least a section of the target sequence, wherein the nucleic acid hybridization thermodynamics are calculated for a plurality of primers or probes complementary to at least a section of the target sequence, wherein the hybridization information represents at least a section of the target sequence and a primer or probe, wherein the length of at least a section of the target sequence is longer than a length of the primer or the probe (column 15, lines 32-41; column 16, lines 1-60; column 3, line 62-column 4, line 59; Figures 5B and 5C; column 5, lines 25-63, column 7,lines 16-29).

Regarding claims 20, 40, and 60, Lane et al. teach wherein the thermodynamics are calculated for at least two best target/primer or target/probe complexes and for their corresponding competitive mismatch complexes and correcting for any interactions

between at least two best target/primer or target/probe complexes and their components (column 45, lines 7-61).

It would have been obvious to combine the references of Lange et al. and Lane et al. given that both methods are drawn to determining hybridization thermodynamics. One of Lane et al.'s stated goals is to determine the free energy-parameter of a duplex formed by the hybridization of a single stranded nucleotide (column 2, lines 40-43). Thus it would have been obvious to one of ordinary skill in the art at the time of the invention to use a method, such as one disclosed by Lange et al., to determine the hybridization potential of two polymers (column 1, lines 15-25). In addition, both methods are implements using computational techniques which one of ordinary skill in the art may combine with ease. Thus it would have been obvious to one of ordinary skill in the art to combine the methods of Lange et al. and Lane et al. given their common goals and common implementation techniques.

Claims 6-8, 26-28, and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lange et al. (US 6,403,314) in view of Lane et al. (US 6,027,884), further in view of Barciszewski et al. (RNA Biochemistry and Biotechnology).

Lange et al. and Lane et al. are applied as above.

Lange et al. or Lane et al. do not explicitly teach using dangling end parameters, coaxial stacking parameters, or terminal mismatch parameters.

Regarding claims 6-8, 26-28, and 46-48, Barciszewski et al. teach using dangling end parameters (p. 21, fourth full paragraph), coaxial stacking parameters (p. 22, first full paragraph), and terminal mismatch parameters (p. 15, third full paragraph).

It would have been obvious to one or ordinary skill in the art to combine the references of Lange et al. and Barciszewski et al. Lange et al. teach a computational method for predicting the hybridization stability of two polymers (see abstract). Barciszewski et al. also teach a computational method that utilizes the thermodynamics of nucleic acids to determine secondary structure (se abstract). Both method are implemented using computational techniques which one of ordinary skill in the art my combine with ease. Lange et al. further state that their method is extremely flexible and can incorporate many different computational methods (column 6, lines 51-60). In addition, one of Lange et al.'s stated goals is to analyze and list all possible single-fragment and multi-fragment cross-hybridizations between a probe molecules and a target molecule and to find the most stable hybridization (column 5, lines 44-56). To achieve Lange et al.'s stated goals, one of ordinary skill in the art would incorporate the method disclosed by Barciszewski et al. to include polymers with dangling ends or terminal mismatches to expand the types of polymers Lange et al.'s method can analyze to find all the possible hybridizations and to find the most stable duplex.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jerry Lin whose telephone number is (571) 272-2561. The examiner can normally be reached on 6:30-5:00, M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D. can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

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MICHAEL BORIN, PH.D
PRIMARY EXAMINER

JL